



PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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INTERNATIO	ONAL PRELIMINARY EXAMINA	TION REPORT
	(PCT Article 36 and Rule 70)	
Applicant's or agent's file reference BIF023280/GP		ation of Transmittal of Intern Examination Report (Form PCT/IPEA
International application No. PCT/FR2003/001328	International filing date (day/month/year) 28 avril 2003 (28.04.2003)	Priority date (day/month/year) 30 avril 2002 (30.04.200)
International Patent Classification (IPC) or no C12N 7/00	ational classification and IPC	
Applicant	INSTITUT PASTEUR	
and is transmitted to the applicant ac 2. This REPORT consists of a total of This report is also accompani amended and are the basis for 70.16 and Section 607 of the These annexes consist of a to		neet. n, claims and/or drawings which hav
IV Lack of unity of inv	of opinion with regard to novelty, inventive stevention t under Article 35(2) with regard to novelty, inventions supporting such statement	·
т Ш	ne international application s on the international application	
VII Certain defects in the	ne international application	f this report
VII Certain defects in the	ne international application s on the international application Date of completion of	f this report otember 2004 (03.09.2004)
VII Certain defects in the VIII Certain observation Date of submission of the demand	ne international application s on the international application Date of completion of	



International Acation No. PCT/FR2003/001328

I. Basis of the report								
1. With regard to the elements of the international application:*								
Į		the inter	he international application as originally filed					
į	\boxtimes	the desc	ription:					
•	_	pages	1-44	, as originally filed				
		pages		, filed with the demand				
		pages	, filed with the letter of					
	\bowtie	the clair	ms:					
'		pages	1-52	, as originally filed				
		pages	, as amended (together	with any statement under Article 19				
		pages		, filed with the demand				
		pages .	, filed with the letter of					
ì	\boxtimes	the drav	wings:					
1		pages	1/5-5/5	, as originally filed				
		pages		, filed with the demand				
		pages	, filed with the letter of					
l	\square	he seave	ence listing part of the description:					
,	"	pages		, as originally filed				
		pages		, filed with the demand				
		pages	, filed with the letter of					
	the in These	the language the l	Iguage of a translation furnished for the purposes of international search (under Ruaguage of publication of the international application (under Rule 48.3(b)). Inguage of the translation furnished for the purposes of international preliminary 3). It o any nucleotide and/or amino acid sequence disclosed in the international axamination was carried out on the basis of the sequence listing: International application in written form. International application in computer readable form. International application in written form. International application in computer readable form. International application in computer readable form. International application as filed has been furnished. International application as filed has been furnished. International application is identical to the purposes of international search (under Ruaguage Authority in the purposes of international preliminary in the purpose	which is: de 23.1(b)). examination (under Rule 55.2 and/ ional application, the international go beyond the disclosure in the				
4.		The an	mendments have resulted in the cancellation of: the description, pages the claims, Nos the drawings, sheets/fig					
5.		This rebeyond	eport has been established as if (some of) the amendments had not been made, sind the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**	nce they have been considered to go				
	in the	is repor 70.17).	sheets which have been furnished to the receiving Office in response to an invita t as "originally filed" and are not annexed to this report since they do no	t contain amenaments (Rule 70.10				
**	Any r	replacem	nent sheet containing such amendments must be referred to under item 1 and anne	xed to this report.				



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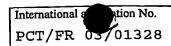
III. Non-establishment f opinion with regard to novelty, inventive step and industrial applicability						
1. The quindustri	estions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be ially applicable have not been examined in respect of:					
	the entire international application.					
\boxtimes	claims Nos					
because	e:					
	the said international application, or the said claims Nos relate to the following subject matter which does not require an international preliminary examination (specify):					
	the description, claims or drawings (indicate particular elements below) or said claims Nos. 38-42, 44-46 are so unclear that no meaningful opinion could be formed (specify): See the separate sheet					
	the claims, or said claims Nos are so inadequately supported by the description that no meaningful opinion could be formed.					
	no international search report has been established for said claims Nos					
2. A mea	aningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acidence listing to comply with the standard provided for in Annex C of the Administrative Instructions:					
	the written form has not been furnished or does not comply with the standard.					
	the computer readable form has not been furnished or does not comply with the standard.					



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IV. Lack of unity f inventi n				
1. In response to the invitation to restrict or pay additional fees the applicant has:				
restricted the claims.				
paid additional fees.				
paid additional fees under protest.				
neither restricted nor paid additional fees.				
This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.				
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is				
complied with.				
not complied with for the following reasons:				
4. Consequently, the foll wing parts of the international application were the subject of international preliminary examination in establishing this report:				
all parts.				
the parts relating to claims Nos				



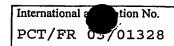
Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III.

Claims 38-42 and 44-46 relate to a method for obtaining polynucleotides of interest including at least one D-base, using a Cyanophage S-2L polypeptide defined in terms of a desirable feature or property, namely that said Cyanophage S-2L polypeptide is "involved in D-base synthesis or is capable of causing, in a host micro-organism, the synthesis of at least one D-base". Such a formulation does not fulfil the requirement of clarity of PCT Article 5 (PCT Guidelines, III-4.7).

The substantive examination is restricted to the subject matter for which the application appears to provide support under the terms of PCT Article 6 and a disclosure under the terms of PCT Article 5, i.e. those parts of the claims that relate to a Cyanophage S-2L nucleotide sequence coding for a succinyladenylate synthetase defined, e.g., by SEQ ID NO: 175 (Table 1) or as described on page 43, line 28 to page 44, line 2.



Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: IV.

1.1. The different inventions are as follows:

Invention 1: the nucleotide sequence of Cyanophage S-2L, characterised in that it corresponds to SEQ ID NO: 1 (claims 1, 49-52 (all in full), 2, 24, 48 (all in part)).

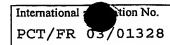
Inventions 2-527: nucleotide sequence coding for a Cyanophage S-2L polypeptide of SEQ ID NO: 2-527 (claims 2-37, 48 (all in part, insofar as they are applicable).

Invention 528: method for obtaining D-bases using Cyanophage S-2L (claims 38-41, 45 (all in part), 43, 47 (all in full)).

Invention 529: method for obtaining polynucleotides of interest including at least one D-base using Cyanophage S-2L (claims 38-41, 45 (all in part), 42, 44, 46 (all in full)).

1.2. These inventions are not so linked as to form a single general inventive concept (PCT Rule 13.1) for the following reasons:

The prior art describes the identification of Cyanophage S-2L and the composition of the DNA thereof, incorporating the D-base (2,6,diaminopurine) instead of the A-base (adenine) (Khudyakov et al, 1977, Kirnos et al, 1977 and Khudyakov et al, 1978, cited on page 3 of the description). These documents disclose that infection with Cyanophage S-2L induces new pathways for synthesising the modified A-bases in cyanobacteria, which



Supplemental Box (To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: IV.

indicates the existence of viral genes involved in the synthesis of modified A-bases. The general concept, the synthesis of D-bases in cells infected by Cyanophage S-2L, is not novel and cannot constitute a single general inventive concept common to the plurality of subjects. Moreover, a person skilled in the art can arrive in an obvious manner at the nucleotide sequence of the genome of a known organism, in this case Cyanophage S-2L, by routine experimentation, without an inventive step being involved. Consequently, the genome nucleotide sequence, the reading frames of each of the Cyanophage S-2L polypeptides and the methods for obtaining D-bases or polynucleotides of interest including at least one D-base using Cyanophage S-2L, are not so linked as to form a single general inventive concept.

In order to move forward with the procedure and despite the lack of unity of invention, a substantive examination was carried out for the two inventions that have been searched (1 and 529).

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7. Reasoned statement under Article 3 citations and explanations supporti		novelty, inventive step or industrial applicability	;
. Statement			
Novelty (N)	Claims	1,2, 24, 38-42, 44-46, 48-52	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1,2, 24, 38-42, 44-46, 48-52	NO
Industrial applicability (IA)	Claims	1,2, 24, 38-42, 44-46, 48-52	- YES
21.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.	Claims		NO

- 2. Citations and explanations
 - 2. Reference is made to the following documents:

D1: KIRNOS M D ET AL: "2 AMINO ADENINE IS AN ADENINE SUBSTITUTING FOR A BASE IN S-2L CYANOPHAGE DNA" NATURE (LONDON), vol. 270, no. 5635, 1977, pages 369-370, XP0002239457 ISSN: 0028-0836, cited in the application

D2: KHUDYAKOV I YA ET AL: "2 6 DI AMINO PURINE A NEW ADENINE REPLACING BASE IN THE DNA OF CYANO PHAGE S-2" DOKLADY BIOCHEMISTRY (ENGLISH TRANSLATION OF DOKLADY AKADEMII NAUK, vol. 232, no. 1-6, 1977, pages 42-45, XP0008016379 1977 ISSN: 0012-4958, cited in the application

D3: KHUDYAKOV I YA ET AL: "CYANOPHAGE S-2L CONTAINS DNA WITH 2 6 DI AMINO PURINE SUBSTITUTED FOR ADENINE" VIROLOGY, vol. 88, no. 1, 1978, pages 8-18, XP008016377 EN ISSN: 0042-6822, cited in the application.

3. Invention 1 (claims 1, 2, 24, 48-52):

Novelty

The genome nucleotide sequence of Cyanophage S-2L corresponding to SEQ ID NO: 1 is novel because it has not been disclosed in the prior art. Consequently, claims 1, 2, 24 and 48-52 are novel (PCT Article 33(2)).

..... Inventive step - - -----

Providing the genome sequence SEQ ID NO: 1 derived from the genome library of Cyanophage S-2L deposited at the CNCM under the reference I-2619, is not considered to be inventive, since a person skilled in the art can arrive in an obvious manner at the nucleotide sequence of a known organism, in the present case Cyanophage S-2L (D1-D3), via routine experimentation without an inventive step being involved.

Claims 1, 2, 24 and 48-52 do not involve an inventive step (PCT Article 33(3)).

4. Invention 529 (claims 38-42 and 44-46)

Novelty

The prior art does not disclose a method for obtaining polynucleotides of interest including at least one D-base using a nucleotide sequence of Cyanophage S-2L coding for a succinyladenylate synthetase defined by SEQ ID NO: 175 (Table 1) or as described on page 43, line 28 to page 44, line 2. Consequently, the subject matter of claims 38-42 and 44-46 is considered to be novel (PCT Article 33(2)).

Inventive step

The present application claims a method for obtaining polynucleotides of interest including at least one D-base using a nucleotide sequence of Cyanophage S-2L coding for a succinyladenylate synthetase, but the effect of using said polynucleotide sequence in said method has not been shown. It appears that the actual invention, the identification of all the polynucleotide sequences required for obtaining polynucleotides of interest including at least one D-base, remains to be achieved.

Therefore, the subject matter of claims 38-42 and 44-46 does not involve an inventive step (PCT Article 33(3)).

PCT Articles 5 and 6

The subject matter of claims 38-42 and 44-46 is a method for obtaining polynucleotides of interest including at least one D-base using a nucleotide sequence of Cyanophage S-2L coding for a succinyladenylate synthetase defined by SEQ ID NO: 175 (Table 1) or as described on page 43, line 28 to page 44, line 2.

However, the application only discloses one example showing the expression of the gene coding for a Cyanophage S-2L succinyladenylate synthetase in Escherichia coli, without providing any evidence of the production of polynucleotides of interest including at least one D-base in these transformed bacteria. The effect of introducing the succinyladenylate synthetase gene in the D-base biosynthesis pathway in the transformed bacteria has not been shown and it appears that several genes of Cyanophage S-2L are necessary to obtain the polynucleotides of interest including at least one D-base, as suggested on

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page 43 (lines 12-20) of the description of the present application.

Consequently, the present application does not set forth the essential features for carrying out the invention to which claims 38-42 and 44-46 are directed, and in a sufficiently clear manner for a person skilled in the art to carry out the invention without undue effort and without exercising an inventive skill. Said claims cannot consequently be considered to be supported under the terms of PCT Article 6 and the application does not provide sufficient disclosure of the invention under the terms of PCT Article 5.